Pharmacokinetic-Pharmacodynamic Analysis of Oral Vancomycin and Gut Microbiome Changes in Healthy Volunteers: An Exploratory Study

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Poster #620

BACKGROUND

- A fixed dose of oral vancomycin 125 mg four times daily is the guideline recommended dosing regimen for *Clostridioides difficile* infection (CDI)[1]
- Oral vancomycin is poorly absorbed systemically leading to high intra-colonic vancomycin concentrations and has a profound impact on the gut microbiome[2]
- However, the relationship between pharmacokinetics of oral vancomycin and pharmacodynamic changes specifically on the gut microbiome has not been explored
- This exploratory sub-study was to investigate fecal vancomycin concentrations in healthy subjects during the early dosing period in relation to the gut microbiome diversity changes

OBJECTIVE

- To investigate fecal vancomycin concentrations in healthy individuals in relation to gut microbiome diversity changes

METHODS

Inclusion criteria

- Healthy subjects aged 18 to 45 years
- No clinically significant past medical history
- No antibiotic use in the 28 days prior to enrollment
- No history of known CDI within the past year

Study design/Sample collection

- Subjects received oral vancomycin 125 mg four times daily for 10 days
- Stool samples were collected at baseline (Day 0) and during antibiotic days

Pharmacokinetic analysis

- High-performance liquid chromatograph (HPLC) assay was used to quantify vancomycin concentrations

Gut microbiome analysis

- Stool DNA was extracted using a DNeasy PowerSoil Pro Kit (Qiagen) in a QiaCube automated DNA extraction system
- Shotgun metagenomic sequencing was performed using the Nextera DNA Flex Library Prep Kit (Illumina) for DNA library preparation and an Illumina NextSeq 500 platform for sequencing
- CLC Genomics Workbench (Qiagen, version 12) was used for metagenomics assembly and analysis

RESULTS

Table 1. Patient Demographics

Characteristics	Subjects (n=6)
Age, mean (±SD), y	31.8 ± 4.5
Male, no. (%)	6 (100%)
Race/ethnicity, no. (%) White, non-Hispanic Black, non-Hispanic	 3 (50%) 3 (50%)
Weight, mean (±SD), kg	86.4 ± 6.8
Body mass index, mean (±SD), kg/m^2	26.8 ± 1.3
Dietary habits, no. (%) Omnivore	 6 (100%)

Figure 1. Fecal Vancomycin Concentrations from Day 0 to Day 4

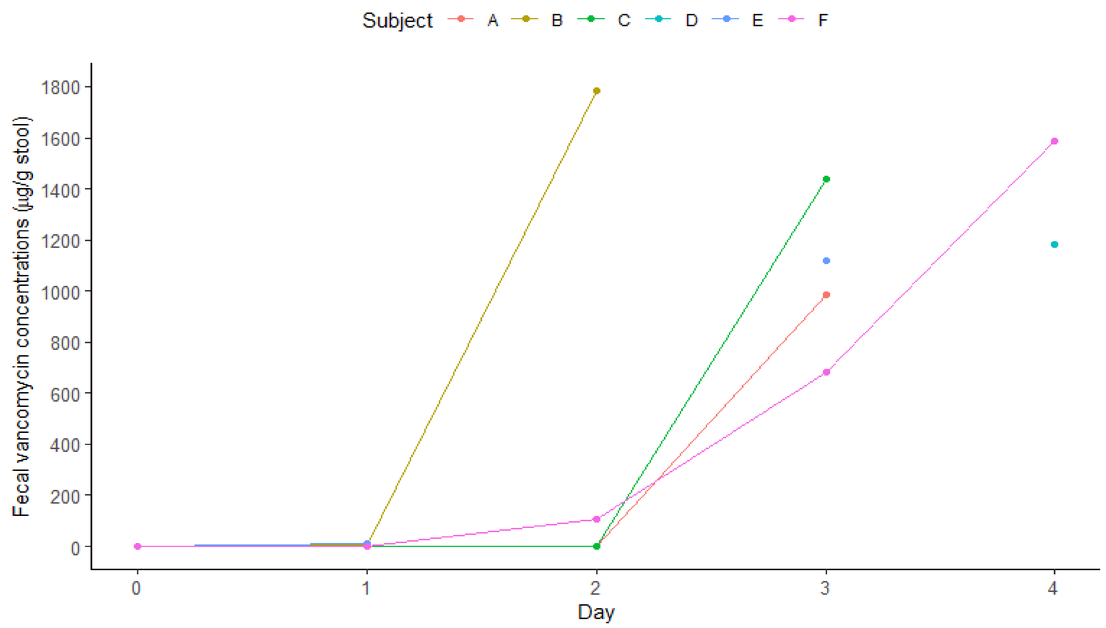
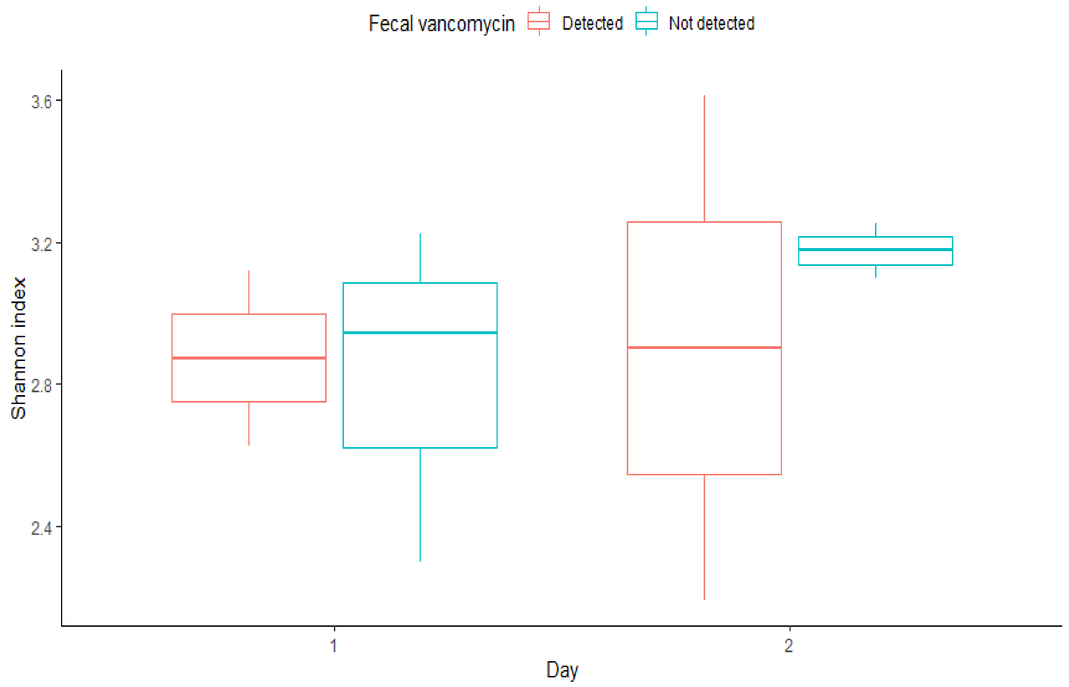


Figure 2. Microbiome Diversity Comparison between Patients with Detectable vs. Non-detectable Fecal Vancomycin Levels



CONCLUSIONS

- Fecal vancomycin concentrations were variable between patients and some were low in the early dosing period
- Proportional, subject-specific differences in gut microbiome diversity and phyla were observed within 24-48 hours of detectable vancomycin levels in the feces
- Future studies are warranted to better understand microbiome changes in the early dosing period of oral vancomycin

FUNDING

This study was funded by Roderick D. MacDonald Research Fund

REFERENCES

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